REMARKS

Restriction Requirement

The Examiner has required restriction of the application to one sequence identified in claim 61 (SEQ ID NOs:1-2189 and 5399-5416), and one sequence identified in claim 62 (SEQ ID NOs: 2190-5398 and 5425-5434). The Examiner has also required restriction of the form of enzymatic nucleic acid (note that these are categories, and not individual species) to one of:

I. Hammerhead;
II. Hairpin;
III. HDV;
IV. Group I intron;
V. VS nucleic acid;
VI. Amberzyme;
VII. Zinzyme;
VIII. RNAse P;
IX. Inozyme;
X. G-cleaver; and
XI. DNAzyme motif.

Applicants elect sequences SEQ ID NOs:143 and 2332, and the enzymatic nucleic acids of Group I (hammerhead), with traverse.

Applicants traverse the requirements on the grounds that the sequences are not separate and distinct inventions. As set forth in MPEP §2434, "**Nucleotide sequences encoding the same protein are not considered to be independent and distinct and will continue to be examined together.**" Applicants respectfully point out that SEQ ID NOs:1-2189 (see Tables I-VIII) and 5399-5416 (Table IX) are all target sequences, and thus are only subsets of the single CLCA1 gene. Thus SEQ ID NOs:1-2189 and 5399-5416 are all parts of a single gene encoding a single protein. Accordingly, SEQ ID NOs:1-2189 and 5399-5416 should all be examined together.

SEQ ID NOs:2190-2764 each correspond to a hammerhead ribozyme complementary to the target sequences of SEQ ID NOs:1-2189. As set forth in Table III, each ribozyme sequence has two sequences complementary to the target sequence, with a functional core region in between. Note in

Table III that the middle three segments (the underlined segment and the segment flanking either side) of each hammerhead sequence are **identical**. The first and last segments of each ribozyme are complementary to the last and first segments, respectively, of the target sequence on the same line. Thus, each ribozyme of SEQ ID NOs:2190-2764 has a sequence complementary to one of SEQ ID NOs:1-2189 (i.e., all are complementary to the same full-length CLCA1 sequence), and has the same functional hammerhead motif inserted in the middle. As ribozymes, these nucleic acids do not encode separate proteins (or any proteins): they are functional as nucleic acids. As they are all active against CLCA1, they do not have separate and individual uses or purposes, and are all closely related by sequence and structure. Thus, restriction between these sequences is not proper or legally supported.

SEQ ID NOs:2765-3399 (Table IV) each correspond to an inozyme complementary to the target sequences. Note again that each inozyme listed has an identical core segment (which, further, is identical to the core sequence of SEQ ID NOs:2190-2764 described above) and two flanking segments that are complementary to two regions of the target sequence, but where the first nucleotide of the last inozyme segment is inosine rather than guanine. As all of the listed inozyme sequences are active against the CLCA1 sequence, they should all be examined together.

SEQ ID NOs:3400-3618 (Table V) each correspond to a G-cleaver motif ribozyme complementary to the target sequences. Note again that each G-cleaver listed has an identical core segment and two flanking segments that are complementary to two regions of the target sequence. As all of the listed G-cleaver sequences are active against the CLCA1 sequence, they should all be examined together.

SEQ ID NOs:3619-3918 (Table VI) each correspond to a zinzyme ribozyme complementary to the target sequences. Note again that each zinzyme listed has an identical core segment and two flanking segments that are complementary to two regions of the target sequence. As all of the listed zinzyme sequences are active against the CLCA1 sequence, they should all be examined together.

SEQ ID NOs:3919-4671 (Table VII) each correspond to a DNAzyme ribozyme complementary to the target sequences. Note again that each DNAzyme listed has an identical core segment and two flanking segments that are complementary to two regions of the target sequence. As all of the listed DNAzyme sequences are active against the CLCA1 sequence, they should all be examined together.

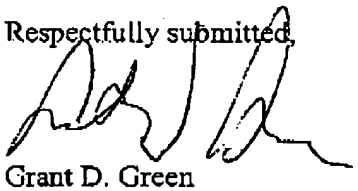
SEQ ID NOs:4672-5398 (Table VIII) each correspond to an amberzyme ribozyme complementary to the target sequences. Note again that each amberzyme listed has a group of identical core segments and two flanking segments that are complementary to two regions of the target sequence. As all of the listed amberzyme sequences are active against the CLCA1 sequence, they should all be examined together.

SEQ ID NOs:5417-5434 (Table IX) each correspond to a GeneBloc sequence, each of which has regions complementary to the target CLCA1 sequence. As all of the listed GeneBloc sequences are active against the CLCA1 sequence, they should all be examined together.

In the case of SEQ ID NOs: 1-2189 and 5399-5416, all sequences may be searched in a single pass, by simply searching the entire CLCA1 sequence and filtering for matches that are at least 17 bases long. This does not impose an undue burden on the USPTO. In the case of SEQ ID NOs:2190-5398, each of these sequences may also be searched easily: the CLCA1 sequence may be searched, and all results with at least 8 consecutive bases selected. The results are then searched for any sequence that also contains the core sequence. This, also, does not impose an undue burden on the USPTO. Thus, three operations should suffice to search all of SEQ ID NOs:1-5398. Since the USPTO guidelines state that **up to 10** independent and distinct sequences is a reasonable number to examine, where all of SEQ ID NOs: 1-2189 and 5399-5416 are considered as one sequence, Applicants traverse the limitation to a single sequence of claim 61 and a single sequence of claim 62. No evidence or explanation has been presented for finding that only a single sequence is a reasonable number of sequences to search, while the MPEP and USPTO policy states that up to 10 sequences constitutes a reasonable number. Restriction to an unjustifiably low number of sequences results in an undue multiplication and proliferation of applications.

Applicants respectfully submit that the application is now in condition for examination. Such action is solicited.

Respectfully submitted,



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